

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/011577

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBASE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/75172 A (UNIVERSITY OF SOUTHERN CALIFORNIA) 11 October 2001 (2001-10-11) claims 1,4,12,15,21-24  tables 1,2 page 1 - page 3 page 5, paragraph 2 - paragraph 3 page 14 page 44, paragraph 2 - paragraph 5 page 47, paragraph 3 - paragraph 4 ----- -/-	18-29, 53,54 1-6, 8-17, 30-52
Y		

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

17 February 2005

Date of mailing of the international search report

28-07-2005

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VIRMANI A K ET AL: "Aberrant methylation of the adenomatous polyposis coli (APC) gene promoter 1A in breast and lung carcinomas." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. JUL 2001, vol. 7, no. 7, July 2001 (2001-07), pages 1998-2004, XP002317188 ISSN: 1078-0432 abstract page 2002 - page 2003 -----	1-6, 8-17, 30-52
A	BURBEE D G ET AL: "EPIGENETIC INACTIVATION OF RASSF1A IN LUNG AND BREAST CANCERS AND MALIGNANT PHENOTYPE SUPPRESSION" JOURNAL OF THE NATIONAL CANCER INSTITUTE, US DEPT. OF HEALTH, EDUCATION AND WELFARE, PUBLIC HEALTH, US, vol. 93, no. 9, 2 May 2001 (2001-05-02), pages 691-699, XP008006020 ISSN: 0027-8874 abstract page 698 -----	
X	NASS S J ET AL: "Aberrant methylation of the estrogen receptor and E-cadherin 5' CpG islands increases with malignant progression in human breast cancer." CANCER RESEARCH. 15 AUG 2000, vol. 60, no. 16, 15 August 2000 (2000-08-15), pages 4346-4348, XP002317187 ISSN: 0008-5472 the whole document -----	7
Y	YAN PEARLLY S ET AL: "Differential distribution of DNA methylation within the RASSF1A CpG island in breast cancer." CANCER RESEARCH. 1 OCT 2003, vol. 63, no. 19, 1 October 2003 (2003-10-01), pages 6178-6186, XP002317459 ISSN: 0008-5472 abstract page 6184 - page 6185 -----	1-6, 8-17, 30-52
A	----- -----	

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## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	AGATHANGGELOU A ET AL: "Methylation associated inactivation of RASSF1A from region 3p21.3 in lung, breast and ovarian tumours." ONCOGENE. 22 MAR 2001, vol. 20, no. 12, 22 March 2001 (2001-03-22), pages 1509-1518, XP008042353 ISSN: 0950-9232 abstract page 1515 - page 1516 -----	1-6, 8-17, 30-52
Y	US 2003/138783 A1 (SUKUMAR SARASWATI ET AL) 24 July 2003 (2003-07-24)  claims 1,2 paragraphs [0010] - [0015] paragraph [0041] -----	1-6, 8-17, 30-52
X	US 6 265 171 B1 (HERMAN JAMES G ET AL) 24 July 2001 (2001-07-24) cited in the application claims 1,12 table 2 sequence 32 -----	18,55
Y	WO 02/081749 A (UNIVERSITY OF SOUTHERN CALIFORNIA; MARKL, ISABEL; JONES, PETER, A; TOM) 17 October 2002 (2002-10-17)  claims 1-6 -----	1-6, 8-17, 30-52
Y	VIJVER VAN DE M J ET AL: "THE NEW ENGLAND JOURNAL OF MEDICINE A GENE-EXPRESSION SIGNATURE AS A PREDICTOR OF SURVIVAL IN BREAST CANCER" NEW ENGLAND JOURNAL OF MEDICINE, MASSACHUSETTS MEDICAL SOCIETY, BOSTON, MA, US, vol. 347, no. 25, 19 December 2002 (2002-12-19), pages 1999-2009, XP008032093 ISSN: 1533-4406 cited in the application the whole document ----- -/-	2-6, 8-17, 30-52

## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	VEER VAN 'T L J ET AL: "Gene expression profiling predicts clinical outcome of breast cancer" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 415, no. 6871, 31 January 2002 (2002-01-31), pages 530-536, XP002259781 ISSN: 0028-0836 cited in the application the whole document -----	
A	US 2002/164715 A1 (JI LIN ET AL) 7 November 2002 (2002-11-07) paragraphs [0065], [0205], [0249] -----	
A	LEON S A ET AL: "FREE DNA IN THE SERUM OF CANCER PATIENTS AND THE EFFECT OF THERAPY" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 37, no. 3, March 1977 (1977-03), pages 646-650, XP001083834 ISSN: 0008-5472 cited in the application the whole document -----	
A	MANNING D L ET AL: "THE ROLE OF FOUR OESTROGEN-RESPONSIVE GENES, PLIV1, PS2, PSYD3 AND PSYD8, IN PREDICTING RESPONSIVENESS TO ENDOCRINE THERAPY IN PRIMARY BREAST CANCER" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 29A, no. 10, 1993, pages 1462-1468, XP001018909 ISSN: 0959-8049 the whole document -----	
P,X	MÜLLER HANNES M ET AL: "DNA methylation in serum of breast cancer patients: an independent prognostic marker." CANCER RESEARCH. 15 NOV 2003, vol. 63, no. 22, 15 November 2003 (2003-11-15), pages 7641-7645, XP002317189 ISSN: 0008-5472 the whole document -----	1-57

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## INTERNATIONAL SEARCH REPORT

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-57 (all partially)

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-57 (all partially)

A nucleic acid molecule or an oligomer comprising at least 18 nt from the gene ESR1, wherein the ESR1 gene sequence is SEQ ID No. 12,13,22 or 23, an array comprising said oligomer, kits, sets, uses of said nucleic acid molecules, oligomers and arrays and methods analysing the methylation status of ESR1.

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2. claims: 1-57 (all partially)

A nucleic acid molecule or an oligomer comprising at least 18 nt from the gene APC, wherein the APC gene sequence is SEQ ID No. 10,11,20 or 21, an array comprising said oligomer, kits, sets, uses of said nucleic acid molecules, oligomers and arrays and methods analysing the methylation status of APC.

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3. claims: 1-57 (all partially)

A nucleic acid molecule or an oligomer comprising at least 18 nt from the gene HSD17B4, wherein the HSD17B4 gene sequence is SEQ ID No. 8,9,18 or 19, an array comprising said oligomer, kits, sets, uses of said nucleic acid molecules, oligomers and arrays and methods analysing the methylation status of HSD17B4.

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4. claims: 1-57 (all partially)

A nucleic acid molecule or an oligomer comprising at least 18 nt from the gene HIC1, wherein the HIC1 gene sequence is SEQ ID No. 6,7,16 or 17, an array comprising said oligomer, kits, sets, uses of said nucleic acid molecules, oligomers and arrays and methods analysing the methylation status of HIC1.

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5. claims: 1-57 (all partially)

A nucleic acid molecule or an oligomer comprising at least 18 nt from the gene RASSF1A, wherein the RASSF1A gene sequence is SEQ ID No. 14,15,24 or 25, an array comprising said oligomer, kits, sets, uses of said nucleic acid molecules, oligomers and arrays and methods analysing the methylation status of RASSF1A.

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/011577

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0175172	A	11-10-2001	AU	5308801 A	15-10-2001
			CA	2404568 A1	11-10-2001
			EP	1283906 A1	19-02-2003
			JP	2004505612 T	26-02-2004
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